APPLICANT(S): ZIV, Ilan et al. SERIAL NO.: 10/585,928

FILED: Page 2

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## AMENDMENTS TO THE CLAIMS

Please add or amend the claims to read as follows, and cancel without prejudice or disclaimer to resubmission in a divisional or continuation application claims indicated as cancelled:

## 1-27. (Cancelled)

28. (Withdrawn) A method for targeting a compound to a cell undergoing **p**erturbation of the **n**ormal **o**rganization of its plasma **m**embrane (PNOM-cell), comprising the steps of:

(i) contacting a cell population comprising said PNOM-cell with a compound or a conjugate comprising said compound, wherein said compound is represented by the structure as set forth in formula (I):

HO 
$$\longrightarrow$$
 OH  $\longrightarrow$  OH  $\longrightarrow$  CH<sub>2</sub>)<sub>n</sub>M  $\longrightarrow$  (CH<sub>2</sub>)<sub>m</sub>  $\longrightarrow$  (I)

including pharmaceutically acceptable salts, metal chelates, solvates and hydrates of the compound represented by the structure as set forth in formula (I), and solvates and hydrates of the salts; wherein each of R and R' groups is independently selected at each occurrence from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl, linear or branched hydroxy-alkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof; n and m each stands independently for an integer of 0, 1, 2, 3 or 4; n and m may be the same or different; M is selected from null, -O-, -S-, and -N(U), wherein U stands for hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ , or  $C_4$  alkyl; x and z each being an integer of 0, 1 or 2, where x and z can be the same or different; y is an integer of 0, 1 or 2; where in the case that y=2, the substituent R' may be the same or different at each occurrence; and D is a marker for diagnostics, hydrogen, hydroxyl, F or a drug;

(ii) thereby targeting said compound to said PNOM-cell within said cell population.

Page 3

29. (Withdrawn) A method according to Claim 28, wherein D is a marker for diagnostics or a drug.

- 30. (Withdrawn) A method according to Claim 29, wherein M is null.
- 31. (Withdrawn) A method according to Claim 28, comprising the steps of:
- (i) contacting a cell population comprising said PNOM-cell with a compound or a conjugate comprising said compound, wherein said compound is represented by the structure as set forth in formula (II):

H

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (II) and solvates and hydrates of the salts; wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl, linear or branched hydroxy-alkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof; n and m each stands independently for an integer of 0, 1, 2, 3 or 4; n and m may be same or different; M is selected from null, -O-, -S- and -N(U), wherein U stands for hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ , or  $C_4$  alkyl; D is a marker for diagnostics, hydrogen or a drug;

- (ii) thereby targeting said compound to said PNOM-cell within said cell population.
- 32. (Previously presented) A compound represented by the structure as set forth in formula II,

HO
$$CH_2)_nM-(CH_2)_mD$$

Page 4

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (II) and solvates and hydrates of the salts; wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl; n and m each stands independently for an integer of 0, 1, 2, 3 or 4; n and m may be same or different; M is selected from null, -O-, -S- and -N(U), wherein U stands for hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ , or  $C_4$  alkyl; and D is a marker for diagnostics, hydrogen or a drug.

- 33. (Previously presented) The compound according to claim 32, wherein M is null.
- 34. (Canceled).
- 35. (Currently Amended) The compound according to Claim 32, represented by the structure as set forth in formula (III):

III

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (III) and solvates and hydrates of the salts; wherein  $R^3$  is hydroxyl or [[ $F^{18}$ ]]  $^{18}F$ ,  $R^4$  is selected from  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$  or  $C_{10}$  linear or branched alkyl, and k is an integer selected from 0, 1, 2, 3, 4 and 5.

36. (Currently Amended) The compound according to Claim 32, represented by the structure as set forth in formula (IV):

Page 5

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (IV) and solvates and hydrates of said salts.

37. (Currently Amended) The compound according to Claim 32, represented by the structure as set forth in formula (V):

$$HO \longrightarrow O$$
 $H_3C \longrightarrow OH$ 
 $(CH_2)_r$ 

V

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (V) and solvates and hydrates of the salts; wherein J is selected from  $[[F^{18}]]$   $^{18}F$  and OH, and r stands for an integer of 4,5,6,7 or 8.

- 38. (Currently Amended) The compound according to Claim 37, wherein r is 5 and J is  $[[F^{18}]]$   $[F^{18}]$ .
- 39. (Currently Amended) The compound according to claim 37, wherein r is 4 and J is  $[[F^{18}]]^{18}F$ .
- 40. (Currently Amended) The compound according to Claim 32, represented by the structure as set forth in formula (VI):

Page 6

VI

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (VI) and solvates and hydrates of said salts; wherein J is selected from hydrogen,  $[[F^{18}]]^{18}F$  and OH.

41. (Currently amended) The compound according to Claim 32, represented by the structure set forth in formula (VII):

VII

including pharmaceutically acceptable salts, hydrates and solvates of the compound represented by the structure as set forth in formula (VII) and solvates and hydrates of said salts, wherein Q is selected from technetium, oxo-technetium, rhenium and oxo-rhenium,  $R^4$  is selected from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , and  $C_6$  linear or branched alkyl, and p stands for an integer, selected from 1, 2, 3, 4 and 5.

42. (Currently amended) The compound according to Claim 32, represented by the structure set forth in formula (IX):

Page 7

IX

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (IX) and solvates and hydrates of said salts; wherein  $R^5$  is selected from hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , or  $C_6$  linear or branched alkyl; q stands for an integer selected from 1, 2, 3, 4 and 5; and Y is a marker for diagnostics comprising a fluorescent label.

- 43. (Previously presented) The compound according to Claim 42, wherein  $R^5$  is  $CH_3$ ; and q is selected from 3, 4, and 5.
- 44. (Previously presented) The compound according to Claim 42, represented by the structure as set forth in formula (X):

Χ

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (X) and solvates and hydrates of said salts.

Page 8

45. (Withdrawn) A method according to Claim 31, wherein said compound is represented by the structure as set forth in formula (XI):

ΧI

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XI) and solvates and hydrates of the salts; wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$   $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl, linear or branched hydroxyalkyl, linear or branched fluoro-alkyl, aryl or heteroaryl composed of one or two rings, or combinations thereof.

46. (Currently Amended) The compound according to Claim 32, [[as]] represented by the structure as set forth in formula (XI):

ΧĪ

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XI) and solvates and hydrates of the salts; wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$   $C_{10}$ , linear or branched alkyl, wherein F is [[F<sup>18</sup>]]  $^{18}$ F or F<sup>19</sup>.

47. (Currently amended) The compound according to claim 32, represented by the structure set forth in formula XIII:

Page 9

## XIII

including pharmaceutically acceptable salts hydrates, solvates and metal chelates of the compound represented by the structure as set forth in formula (XIII) and solvates and hydrates of the salts; wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$ ,  $C_{10}$ ,  $C_{11}$ ,  $C_{12}$ ,  $C_{13}$ ,  $C_{14}$ ,  $C_{15}$  or  $C_{16}$  linear or branched alkyl, m stands for an integer of 0, 1, 2, 3 or 4; D is a marker for diagnostics or a drug to be targeted to PNOM-cells.

48. (Currently Amended) The compound according to claim 47, wherein R represents hydrogen or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$ ,  $C_9$  or  $C_{10}$  linear or branched alkyl; m is 2 and D is  $[[F^{18}]]$   $^{18}F$ .

49. (Currently Amended) The compound according to Claim 47, represented by the structure set forth in formula (XIV):

## XIV

including pharmaceutically acceptable salts, hydrates, solvates and metal chelates, of the compound represented by the structure as set forth in formula (XIV) and solvates and hydrates of the salts; wherein F is <sup>18</sup>F.

Page 10

50. (Previously presented) The compound according to the structure set forth in any of the formulae III, IV, V, VI, VII, IX, X, XI, XIII, or XIV, comprising or being linked to a marker for imaging.

- 51. (Previously presented) The compound according to claim 50, wherein said marker is Tc, Tc=O, In, Cu, Ga, Xe, Tl, Re and Re=O,  $^{123}$ I,  $^{131}$ I, Gd(III), Fe(III), Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, Mn(II)  $^{18}$ F,  $^{15}$ O,  $^{18}$ O,  $^{11}$ C,  $^{13}$ C,  $^{124}$ I,  $^{13}$ N,  $^{75}$ Br, Tc-99m or In-111.
- 52. (Previously presented) The compound of according to claim 32, wherein said marker for diagnostics comprises Tc, Tc=O, In, Cu, Ga, Xe, Tl, Re and Re=O,  $^{123}$ I,  $^{131}$ I, Gd(III), Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, Mn(II)  $^{18}$ F,  $^{15}$ O,  $^{18}$ O,  $^{11}$ C,  $^{124}$ I,  $^{13}$ N,  $^{75}$ Br, Tc-99m or In-111.
- 53. (Previously presented) The compound according to claim 50, wherein said marker for imaging is detectable by a detector of color, fluorescence, x-ray, CT scan, magnetic resonance imaging (MRI), radio-isotope scan, single photon emission tomography (SPECT) or positron emission tomography (PET).
- 54. (Previously presented) The compound according to claim 32, wherein said marker for diagnostics is detectable by a detector of color, fluorescence, x-ray, CT scan, magnetic resonance imaging (MRI), radio-isotope scan, single photon emission tomography (SPECT) or positron emission tomography (PET).
- 55. (Withdrawn) A pharmaceutical or a diagnostic composition, comprising as an active ingredient an effective amount of a compound according to the structure set forth in any of the formulae III, IV, V, VI, VII, IX, X, XIII, or XIV and a pharmaceutically or diagnostically acceptable carrier.
- 56. (Withdrawn) A method for targeting a compound to a cell undergoing **p**erturbation of the **no**rmal **o**rganization of its plasma **m**embrane (PNOM-cell), comprising the steps of:
- (i) contacting the cell population comprising said PNOM-cell with a compound represented by the structure set forth in any of the formulae III, IV, V, VI, VII, IX, X, XI, XIII, or XIV or a pharmaceutical composition comprising said compound;
- (ii) thereby targeting said compound to said PNOM-cell within said cell population.

APPLICANT(S): ZIV, Ilan et al.

SERIAL NO.: FILED:

10/585,928 July 13, 2006

Page 11

57. (Withdrawn) A method according to Claim 56, wherein said PNOM-cell is a cell

undergoing a cell death process.

58. (Withdrawn) A method according to Claim 28, wherein said PNOM-cell is a cell

undergoing a cell death process.

59. (Withdrawn) A method according to Claim 31, wherein said PNOM-cell is a cell

undergoing a cell death process.

60. (Withdrawn) A method according to Claim 57, wherein said cell death process is

apoptosis.

61. (Withdrawn) A method according to Claim 58, wherein said cell death process is

apoptosis.

62. (Withdrawn) A method according to Claim 59, wherein said cell death process is

apoptosis.

63. (Withdrawn) A method for detecting a PNOM-cell within a cell population, said

method comprising:

(i) contacting the cell population with a compound or a pharmaceutical composition

comprising said compound, wherein said compound is represented by the structure set

forth in any of formulae I, II, III, IV, V, VI, VII, IX, X, XI, XIII, or XIV, comprising or

being linked to a marker for diagnostics; and

(ii) determining the amount of said compound bound to said cells, wherein detection

of a significant amount of said compound bound to a cell indicates its being a PNOM-

cell.

64. (Withdrawn) A method for imaging PNOM-cells in a subject, human or an animal,

comprising:

(i) administering to said subject, human or an animal a compound or a pharmaceutical

composition comprising said compound wherein said compound is represented by the

structure set forth in any one of formulae I, II, III, IV, V, VI, VII, IX, X, XI, XIII, or XIV,

comprising or being linked to a marker for imaging; and

APPLICANT(S): ZIV, Ilan et al.

SERIAL NO.:

10/585,928 July 13, 2006

FILED: Page 12

(ii) imaging the human or animal, so as determine the amount of said pharmaceutical

composition or said compound bound to cells, wherein imaging of a significant amount

of said compound bound to cells indicates their being PNOM-cells.

65. (Withdrawn) The method of Claim 64 for determining of a disease process, a focus

of tumor, or a response to treatment of a disease, in a human or non-human subject,

wherein said disease process, focus of tumor, or response to treatment is associated

with occurrence of cells undergoing a cell death process.

66. (Withdrawn) A method according to Claim 65, wherein said cell death process is

apoptosis.

67. (Withdrawn) A method for targeting a cytotoxic drug to a tumor which has cells

undergoing cell death, said method comprising the step of administering a compound as

represented by a structure set forth in any of the formulae I, II, III, IV, V, VI, VII, IX, X,

XI, XIII, or XIV, comprising or being linked to the cytotoxic drug, thereby targeting of

the cytotoxic drug to the cells undergoing cell death within the tumor.

68. (Withdrawn) A PMBC-PET precursor, represented by a structure as set forth in any of

the formulae I, II, III, V, VI, IX, X, XI, XIII or XIV, comprising or being linked to a moiety

to be substituted by an <sup>18</sup>F radio-isotope upon radio-labeling, thereby generating an <sup>18</sup>F-

labeled compound.

69. (Withdrawn) A PMBC-PET precursor according to Claim 68, wherein said moiety

is a sulfonate, a nitro, a halogen, or a hydroxyl group.